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Giardiasis

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INTRODUCTION

Giardia lamblia was first discovered in 1681 by Antonie van Leeuwenhoek, who found the parasite in his own stools. For many years, *G. lamblia* was considered to be of doubtful pathogenicity. Increased awareness of this parasite and appreciation for its clinical significance surfaced in the early 1970s with its recognition in a large percentage of visitors to the Soviet Union who returned with symptomatic giardiasis (9, 78). Giardiasis caused by *G. lamblia* is now recognized as a disease of travelers worldwide, particularly in the developing world (80). In the United States, *G. lamblia* causes intestinal disease in persons drinking contaminated water (3, 17), in children in day-care centers (57), and in homosexual males (63). *G. lamblia* is currently the most frequently identified pathogen in all waterborne outbreaks in the United States (16). This organism is endemic throughout the world, with the highest prevalence occurring in the tropics and subtropics (38).

ETIOLOGIC AGENT

G. lamblia is a flagellate within the order Retortomonadida and alternates between trophozoite and cyst stages in its life cycle. The trophozoite is pear shaped and dorsally convex and has a shallow, ventral concave sucking disk. The dorsal surface apparently provides an area for diffusion of nutrients (38). Attachment of the sucking disk to the mucosal surface is thought to be from negative pressure which develops in the concavity, in association with beating of the flagella (55). The trophozoite is 9.5 to 21 μm long by 5 to 15 μm wide and has two nuclei and four pairs of flagellae. The appearance of the trophozoite is that of a teardrop when viewed dorsoventrally and spoon shaped when viewed from the side. The positions of the nuclei, median bodies, and axonemes resemble a human "face." The trophozoites exhibit an erratic tumbling motion described as "falling leaf motility." Trophozoites divide by longitudinal binary fission, and cysts develop as liquid feces gradually dehydrate in transiting the large bowel. Cysts are oval with a tough hyaline cyst wall and measure 8 to 12 μm long by 7 to 10 μm wide. The mature cyst contains four nuclei, usually situated at one end; curved median bodies; and the linear axonemes. The cysts can survive if kept cool and damp and have been shown to survive in water for up to 3 months (38). They can also survive standard concentrations of chlorine used in water purification systems (38).

The cysts are ingested with contaminated food or water or are acquired from unwashed hands and pass through the stomach unharmed. Excystation occurs in the duodenum, and the two trophozoites from each mature cyst establish themselves among the intestinal villi (38).

G. lamblia inhabits the duodenum and upper jejunum, where the alkaline pH is favorable for growth. Trophozoites firmly attach to the intestinal microvillus surface with their sucking disks or move about free in the lumen; actual invasion of the mucosa and submucosa has been documented infrequently (8, 62). The trophozoites are most often found in liquid or soft stools and the more resistant, infective cysts are seen in more formed stools.

Giardia trophozoites have been classified into three groups on the basis of morphologic criteria: *G. agilis*, *G. muris*, and *G. duodenalis*. Different strains of *G. duodenalis* (including *G. lamblia*) have been typed by using isoenzyme analysis (5, 48), endonuclease restriction analysis of DNA (54a), and response to in vitro excystation and culture techniques (49). These studies suggest that intraspecific variation occurs within this morphologic group. Recognition of isolate differences may also be important in delineating the pathogenesis of infection. Recently, it has been found that human source *Giardia* isolates produce different patterns of clinical disease and immune response in their gerbil hosts (1, 54). In another study using isoelectric focusing of trophozoite protein from 10 human and animal source *Giardia* isolates, the authors report differences in banding patterns, thus confirming the heterogeneity of this morphological group of *Giardia* spp. (31). Total protein studies have also shown that predictable banding patterns are not seen when strains from human and animal hosts residing in a limited geographical area are examined (31, 48, 54a). Comparison of defined trophozoite proteins rather than total cell proteins may be more informative because of the complex banding patterns demonstrated by the latter.

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EPIDEMIOLOGY

Giardiasis occurs worldwide, with higher prevalence where sanitation is poor. Persons of all ages are affected, though in endemic areas infection is more frequent in infants. Specific areas of recognized increased risk for travelers include the Soviet Union, Southeast and South Asia, tropical Africa, Mexico, and western South America (80). Giardiasis is the most commonly reported pathogenic protozoan disease in the United States (29).

Infection is spread directly from person to person by fecal-oral contamination with cysts or indirectly by transmission in water (3, 17) and occasionally food (55a). Travelers often become infected when they ingest contaminated water that usually originates from groundwater (wells) or surface water (lakes or streams). In the United States, most infections are sporadic, especially in campers and hikers who drink untreated stream water (3). Numerous community-wide outbreaks have resulted from fecally contaminated central water supplies (17). *G. lamblia* is frequently identified as the etiologic agent in waterborne diarrheal outbreaks from contaminated surface water that has been ineffectively filtered or pretreated (29). Thus, contaminated water sources include unfiltered surface waters, shallow wells, and household water from either of these sources (12, 29). Infections occur in outbreak and endemic forms within nursery schools and other institutional settings and among family members of infected children (57). Transmission also occurs among male homosexuals engaging in oral-anal sexual practices (63). Ingestion of 100 or more cysts is required to ensure infection in humans, but ingestion of as few as 10 cysts has resulted in infection in volunteers (58).

Humans are the main reservoir of the parasite, but a variety of animals carry *Giardia* spp. similar to those infecting humans. At first, the genus was thought to contain numerous host-specific species; however, it is now believed that perhaps only two morphologically distinct species infect animals. One of these, *G. duodenalis* (includes *G. lamblia*) naturally infects humans, beavers, coyotes, cattle, cats, and dogs and can experimentally infect certain other mammals. Whereas studies analyzing isolates of *G. duodenalis* from different hosts suggest that intraspecific variation occurs within the group, host specificity is still considered unreliable as a means of classifying *Giardia* spp. The other morphologically distinct species, *G. muris*, infects primarily mice and rats (66). Community water supplies can be contaminated by *G. duodenalis* cysts from beavers, which have been infective for humans experimentally (18a). Experimental infection of dogs has been induced by cysts from humans, but so far there is no documented evidence of transmission from dogs to humans (30a).

PATHOLOGY AND PATHOGENESIS

In asymptomatic infected persons, histologic study of the duodenal and jejunal mucosa usually shows no abnormality. In symptomatic persons, findings may include villous atrophy, crypt hyperplasia, epithelial cell damage, and extensive infiltration of the lamina propria by plasma cells, lymphocytes, and polymorphonuclear leukocytes. Invasion of the mucosa or submucosa has been demonstrated, but is an unusual finding (8). Biopsies at various sites may show a patch distribution of parasites on villi and in intervillous spaces, and giardiasis has been associated with blunting of the microvillous border of epithelial cells. Patients with symptomatic giardiasis can have a normal jejunal histological appearance with no inflammatory exudate (8).

Although the trophozoite stage of *G. lamblia* is thought to interfere with the integrity of the brush border of the upper small intestine, the specific pathogenic mechanisms remain unclear. It is also not yet understood why some infected individuals remain asymptomatic while others become quite ill. Some reports suggest that the trophozoites produce mechanical obstruction by blanketing the intestinal mucosa, thus blocking absorptive activities related to fats and fat-soluble vitamins (50). Some attribute villous and mucosal irritation to direct attachment of the organism via the sucking disk (50, 55). It has also been suggested that infectivity and symptomatology may be related to synergistic activity between *G. lamblia* and enteric bacterial and fungal flora (24, 52a, 73). However, in a study of experimental human infection with *Giardia* trophozoites, there was no correlation between the presence or amount of bacteria and yeasts and infection or the development of symptoms (54). Opinions differ concerning a possible correlation between intraepithelial lymphocytic infiltration and malabsorption (7, 19, 50, 62). Some investigators have postulated that pathogenicity may vary with strains and that some *G. lamblia* strains may produce an enterotoxin (43). Other studies have shown that mucosal damage can give rise to deficiencies of lactase, xylase, and sucrase (26, 70). Reduced digestion and absorption of solutes may then cause osmotic diarrhea with gas formation resulting from bacterial breakdown of sugars.

Studies on host defense mechanisms indicate that individuals with diminished gamma globulin levels have a higher prevalence of infection (2). However, such differences in infected individuals and healthy controls have not always been demonstrated (37). Also, individuals with hypochlorhydria and achlorhydria tend to be more susceptible to giardiasis (23). Various host factors, including diet, bowel motility, and nutritional status, as well as innate characteristics of the parasite, are probably responsible for the pathogenesis of giardiasis. Effects of parasites would include mechanical, toxigenic, and immunologic factors and possible synergistic interactions with other intestinal flora.

IMMUNOLOGY

It is well accepted that both humoral and cellular immune responses to giardial infection are generated by the host. Secreted immunoglobulin A (IgA) and IgM antibodies seem to play a role in eradicating parasites. IgA and IgG antibodies coat *G. muris* trophozoites in the bowel lumen of rats and mice and may reduce parasite motility and prevent adhesion to the epithelium (21). *Giardia*-specific IgG and IgM antibodies have also been demonstrated in serum and may be helpful in differentiating patients with acute or recent infection from those with past or previously treated infections (38). Studies also indicate that, during waterborne outbreaks of diarrheal illness, the presence of serum antibody of *G. lamblia*, particularly IgA, may be helpful in detecting exposure to *G. lamblia*-contaminated water and in diagnosing giardial disease (6).

Experiments with a mouse model have demonstrated that T-cell function is necessary for development of resistance to infection (59, 71). It has also been shown that, after epidemic outbreaks, patients develop some resistance to subsequent infection (32, 83). However, even after repeated exposure to the organism, symptomatic infections do recur in the same individuals. Current evidence suggests that, by adulthood, a degree of resistance to this organism is present. One study

found that 14% of a group of asymptomatic adults had serum antibodies to *G. lamblia* (67).

CLINICAL FEATURES

Symptomatology differs from person to person, depending on such factors as inoculum size, duration of infection, and individual host and perhaps parasite factors. The incubation period generally varies from 9 to 15 days. The acute stage usually begins with a feeling of intestinal uneasiness, followed by nausea and anorexia. Low-grade fever and chills may also be early symptoms. Subsequent symptoms may include explosive, watery, foul-smelling diarrhea; marked abdominal gurgling and distention associated with the passage of foul gas; and perhaps belching, with a foul taste. Upper or mid-epigastric cramps may also occur. Blood and mucus in the stool are rare. The acute stage, which lasts 3 or 4 days, can resemble other causes of traveler's diarrhea and is often not recognized as being due to giardiasis. While most patients experience diarrhea during this time, some of the other symptoms occur less frequently.

Although some acute infection may clear spontaneously, a long-standing subacute or chronic infection may develop. This phase may involve 2 or more years of intermittent diarrhea. In individuals returning from endemic areas, the acute stage may not be remembered, and these patients can present with persistent or recurrent mild to moderate symptoms. During this chronic phase, lassitude, headache, and myalgia may occur with continued weight loss, anorexia, and malabsorption. Chronic infection in children may present as failure to thrive (10, 14). Urticaria (79), cholecystitis (68), and pancreatitis (44) have been reported with *Giardia* infections. Uncommon associated symptoms including arthritis (65) and retinal arteritis and iridocyclitis (42) have responded to specific anti-*Giardia* treatment. As stated by an experienced worker in the field, "the symptomatology of giardiasis is rich and unpredictable; individual variability and the intermittent nature and changing of the symptoms are characteristic" (36).

Many infections disappear after variable periods of time, and about 13% of infected adults and up to 50% of infected young children remain asymptomatic. The duration of the asymptomatic cyst-passing state has not been determined.

In patients with giardiasis, the hemogram is usually normal and eosinophilia is rare. Malabsorption of fat, glucose, lactose, xylose, vitamin A, and vitamin B_{12} has been shown in some patients (13, 25, 50). Clinical symptoms seen in a group of recently infected individuals and in another group with undetermined duration of proven infection are listed in Table 1.

Lactose intolerance, frequently present during infection, may persist for variable periods following apparent eradication of giardiasis with specific treatment. Because this symptom often occurs in individuals from ethnic groups who are predisposed to lactose intolerance, the need for further anti-*Giardia* treatment must be carefully considered, especially in those with negative post-treatment specimens who have persistent typical giardiasis symptoms.

TABLE 1. Clinical features of 32 patients with proven giardiasis recently returned from the Soviet Union compared with 105 State Department cases with undetermined duration of proven infection[a]

Symptom	% with symptom	
	State Department	USSR
Flatulence	46.7	56.5
Foul stool	44.8	52.2
Cramps	32.4	59.4
Distention	31.4	0
Anorexia	20.0	56.2
Nausea	20.0	59.4
Weight loss	18.1	0
Belching	15.2	30.4
Heartburn	14.3	0
Headache	11.4	0
Constipation	11.4	0
Vomiting	4.8	34.4
Fever	3.8	17.4
Chills	2.9	0
Diarrhea	62.9[b]	71.9
Blood in stool	0	0
Mucus in stool	3.8	4.4
Fatigue	28.6	87.5

[a] From reference 82 with permission.
[b] 52.4% had soft or mushy stools; 10.5% had watery stools.

DIAGNOSIS

Most, but not all, cases of giardiasis can be confirmed by stool examination. A series of three stools, one collected each day on alternate days or within no more than 10 days, is recommended. Physicians and laboratorians need to recognize that *Giardia* cysts and trophozoites are shed in the stool on a periodic basis, and even examination of a series of six or more stools may not reveal the organisms. Continued negative stool examinations do not rule out *G. lamblia* as the causative agent.

Although examination of a fresh stool allows motile trophozoites to be seen in a direct wet saline preparation, the use of collection kits containing stool preservatives is recommended for inpatients and is mandatory for outpatient stool collections. If left unpreserved for too long, the organisms tend to disintegrate, thus preventing recognition of the typical trophozoite morphology. A number of kits with preservative solutions are available which can be purchased commercially. These preservatives include 10% buffered formalin, polyvinyl alcohol, merthiolate-iodine-formalin, and sodium acetate-acetic acid-formalin. The most commonly used collection kit contains 10% buffered formalin with which the formalin-ethyl acetate concentration is performed and polyvinyl alcohol from which the permanent stained smear is prepared. Other workers prefer merthiolate-iodine-formalin or sodium acetate-acetic acid-formalin; some find that permanent stained smears of consistent quality may be more difficult to prepare with these solutions.

Purging the patient does no increase the diagnostic yield (11). In given populations of *Giardia*-infected individuals, high, low, and mixed patterns of cyst excretion are observed (18). It has been suggested that confirmation of infection, particularly in low cyst excretors, might require two or three stool examinations per week for 4 or 5 weeks. However, this intensive workup is neither practical nor cost-effective, even in an outpatient setting. Therefore, not all infections in persons with giardiasis, including those with typical symptoms, can be confirmed by using the standard series of three stool examinations, even when recommended collection methods are used and specimens are examined by trained experts.

If organisms are present, the cyst stage is more likely to be seen in stool samples, particularly when the patient does not have diarrhea. Cysts are round to oval with four nuclei,

curved median bodies, and linear axonemes. On direct wet saline preparations, the organisms may appear refractile at ×100 magnification, but some morphologic details can be seen with ×450 magnification (high dry power). Because the cysts are three-dimensional, not all of the internal structures are visible at any one plane of focus. Occasionally, the organism will appear to have shrunk away from the cyst wall and the internal morphology will not be visible. However, the general cyst shape is very suggestive; unless the specimen is old and the organisms are beginning to disintegrate, some cysts usually exhibit the typical morphology. The internal structures may be seen more clearly if iodine solution is added to the preparation. The combination of shape, size, and internal structures will allow *Giardia* cysts to be differentiated from those of other intestinal protozoa or possible artifact material.

Unless the patient has acute diarrhea, it is usually much less common to see the trophozoite stage in the stool specimen. Although most books describe the typical falling-leaf motility of the trophozoite, the organisms are often caught up in microscopic bits of mucus and the only visible motility may be the flutter of flagella. Trophozoites are described as teardrop shaped from the front and curved from the side, and they have a face that looks back at the examiner. The trophozoites in a direct wet preparation can be missed if the light is too bright. One may have to look at each field for a few seconds with reduced lighting to see the organisms. The addition of Lugol's or D'Antoni's iodine can be helpful, although the iodine will kill the trophozoites, thus eliminating the possibility of seeing motile organisms. Some workers think that performing a direct wet examination on preserved material is an inefficient use of technologist time and that specimens submitted in stool preservatives should be examined only with concentration and permanent, stained-smear procedures.

In some cryptic cases unable to be confirmed by stool examinations, examination of fluid from the area of the duodeno-jejunal junction may reveal *Giardia* trophozoites. Fluid can be obtained by endoscopy or, more simply, by using the duodenal string test (Entero-Test) (4). The Entero-Test is a gelatin capsule containing a length of nylon string to which a small weight is attached. On ingestion, the capsule dissolves, the nylon string is released, and peristaltic action pulls the weighted string down into the duodenal area. While the string is in place, the patient can drink some water, but food should not be eaten. The end of the string is usually taped to the patient's cheek during the recommended 4-h test time. When the string is retrieved, the weight is released, passes through the intestinal tract, and is eliminated with the feces. The mucus and fluid from the bile-stained portion of the string are removed by pulling the string through pinched fingers of a gloved hand. Several drops of mucus are usually obtained. Most workers examine the material as a direct wet smear preparation (using low light intensity and the ×40 objective). The typical falling-leaf motility that is often described for *Giardia* trophozoites is rarely seen in this type of preparation because the organisms are caught up in mucus. Again, the only motility visible may be a slight flutter of flagellae. Once an organism is found, the rest of the material can be fixed directly on the slide (1 drop of mucus mixed with 3 drops of polyvinyl alcohol), air dried, and then stained for a permanent mount.

Reports on the value of duodenal fluid examination are mixed; some workers report it to be more reliable than stool examinations (39), while others have shown that stools may be positive when duodenal fluid and biopsy examinations are negative (52). Until more conclusive information is available, this examination should supplement, but not replace, the stool examination (22).

TABLE 2. Possible problems preventing identification of *G. lamblia*[a]

Problem	Comment
Medication administration	Antibiotics may cause organism distortion or organisms may be present in very low numbers; antacids, antidiarrheal preparations, laxatives may cause organism distortion or may mask their presence
Diagnostic procedures	Enemas may cause organism distortion
Radiographic examination	Barium may cause organism distortion and mask their presence
Intermittent shedding	Organism numbers in stool fluctuate widely
Specimen collection	Trophozoites may disintegrate without fixative
Laboratory techniques	Use of concentration techniques and permanent stained fecal smears are mandatory for complete stool workup
Specimen examination	Trained personnel required for accuracy
Failure to obtain additional specimen types	Duodenal drainage/aspirates/biopsy; use of the Entero-Test capsule technique; EIA technique to detect fecal antigen

[a] From references 19, 22, 56, and 75.

In an occasional case of giardiasis that cannot be confirmed by the above methods, diagnosis may be made by small intestinal biopsy in the area of the duodeno-jejunal junction or, preferably, from multiple duodenal and jejunal sites. Imprint smears for Giemsa stain should be prepared from the biopsies before they are submitted for routine histologic examination (2, 11). The morphology of the organisms in these preparations may be considerably more distorted than in routine, permanently stained, fecal smears. *G. lamblia* is rarely recognized as a mucosal invader; therefore, parasites are more likely to be found on the microvillus border, particularly in the crypts.

Upper gastrointestinal tract radiography studies with barium sulfate are abnormal in about 20% of infected individuals and may demonstrate irregular thickening of the mucosal folds; spasticity of the gut, particularly in the duodenum and proximal jejunum; and fragmentation of the barium column due to increased intestinal secretions (47). Although not specific for giardiasis, these findings suggest the diagnosis in a clinically suspect case. Barium examination is best preceded by examination of stool, intestinal fluid, or biopsy material, because of the difficulty in recognizing intestinal protozoa for at least 1 week after its use. Similarly, many antimicrobial agents, antacids, kaolin products, bismuth subsalicylate, enema products, and oily laxatives may temporarily interfere with parasite recovery. Possible reasons for the failure to recover *Giardia* organisms are listed in Table 2.

It is well known that humoral and cellular host responses are generated, and serum antibodies have been demonstrated by using enzyme immunoassay (EIA) (27). Serum anti-*G. lamblia* IgM is short-lived when compared with serum anti-*G. lamblia* IgG (27). This difference may assist the clinician in separating patients with acute or recent

TABLE 3. Rapid detection assays for *G. lamblia*[a]

Authors (reference)	Assay	Detection	Sensitivity (%)	Specificity (%)
Craft and Nelson (15)	CIE	Ag	98	—[b]
Venayak et al. (76)	CIE	Ag	94	95
Rosoff and Stibbs (60, 61)	CIE	Ag	90	—
Ungar et al. (75)	EIA	Ag	92	98
Green et al. (30)	EIA	Ag	98	100
Nash et al. (53)	EIA	Ag	95	—
Knisley et al. (41)	EIA	Ag	92	87
Stibbs et al. (72)	EIA	Ag	92	—
Kneip and Topping (40)	IIF	Cyst	97	100
Janoff et al. (33)	CIE	Ag	88	97
	EIA	Ag	94	95

[a] CIE, counterimmunoelectrophoresis; IIF, indirect immunofluorescence; Ag, antigen.
[b] —, not determined or not given.

giardiasis from those who have had past exposure or treated disease. Unfortunately, commercially produced kits for the detection of humoral antibodies are not available.

Counterimmunoelectrophoresis (15) and EIA techniques (53, 75) have been used to detect fecal antigen in both fresh and formalin-preserved stool specimens (72). Several kits containing monoclonal antibodies are available for antigen detection by the double-antibody sandwich EIA technique and for detection of intact organisms by indirect immunofluorescence (69). The indirect immunofluorescence reagent is also effective for detecting *Giardia* sp. cysts in frozen fecal samples in which freezing and thawing may distort cysts and prevent their detection by bright-field microscopy (20). Immunologic tests may be of particular benefit for screening patient specimens, either when giardiasis is suspected or in outbreak situations. One product that is available combines monoclonal antibodies for the detection of *Giardia* and *Cryptosporidium* oocysts (Meridian Diagnostics, Cincinnati, Ohio). This combination reagent is being used for water testing and in selected patient populations. Each institution needs to determine the need for such testing on the basis of considerations such as patient population, input from the medical staff, need to offer screening methods, approach to batch testing, availability of necessary equipment and personnel, priority of test among all tests offered, and cost. In-service presentation is mandatory to ensure that the clinical relevance and limitations of such immunologic tests are thoroughly understood by the staff involved. A comparison of rapid detection assays is presented in Table 3.

Different workers have had various rates of success with the diagnostic methods cited (Table 4). In part, these differences are related to technical expertise and care used in performing the tests and quality of reagents. It is evident that no method or combination of methods can detect all *Giardia* infections. In patients with strong clinical and epidemiological evidence of giardiasis, marked improvement and apparent cure may follow empiric treatment with specific anti-*Giardia* drugs despite negative diagnostic tests.

DIFFERENTIAL DIAGNOSIS

Acute diarrhea from giardiasis must be differentiated from that caused by viruses, bacteria, and other protozoa. Giardiasis has a longer incubation period than most other enteric infections and should be suspected in patients with upper abdominal discomfort and distention, foul stool, and gas. Characteristically, blood or mucus are not present in the stool. Chronic diarrhea from giardiasis must be differentiated from infections caused by *Entamoeba histolytica*, *Dientamoeba fragilis*, *Cryptosporidium parvum*, *Isospora belli*, and *Strongyloides stercoralis* as well as malabsorption, irritable bowel syndromes, and inflammatory bowel disease. Giardiasis may also mimic duodenal ulcer, hiatal hernia, and gallbladder or pancreatic disease. If peripheral blood eosinophilia is present, symptoms are unlikely to be due to giardiasis, and other parasites, particularly helminths, should be suspected.

TABLE 4. Clinical Relevance and Efficacy of Various Techniques for the Diagnosis of Giardiasis[a]

Examination	Results
Direct wet prepn	Significant differences in sensitivity reported
Merthiolate-iodine-formalin concentrate	Better than Lugol's iodine and methylene blue wet mounts for cysts
Trichrome stain	Better than Lugol's iodine and methylene blue wet mounts for cysts; best for trophozoites
Small bowel aspirate	May be helpful in organism recovery when stools are negative, but this procedure does not take the place of ova and parasite examinations
Endoscopic brush cytology	May be helpful
Small bowel biopsy	Optimal: stain touch preparation of mucus with Giemsa or Masson's trichrome stain
Antigen detection	High specificity and sensitivity reported
Antibody detection	May be useful in distinguishing acute or chronic infection, if available

[a] From references 19 and 22.

TREATMENT

Drugs available in the United States for treatment of giardiasis include metronidazole, quinacrine, and furazolidone. A number of nitroimidazole compounds, including tinidazole, ornidazole, and nimorazole, have also been found effective, but are not available in the United States.

Metronidazole (Flagyl) is given in doses of 250 mg three times a day for 7 days for adults and 5 mg/kg three times a day for 7 days for children. Cure rates are in the range of 85 to 95%. Metronidazole is somewhat less effective than quinacrine, but is usually better tolerated. Side effects can include a metallic taste, dark urine, occasional gastrointestinal symptoms, and candidal overgrowth in the bowel. The patient should not consume alcohol while under treatment with metronidazole or quinacrine because of an Antabuse-like effect of these drugs. Questions regarding potential carcinogenic and mutagenic effects of metronidazole have arisen, but careful observation and follow-up of treated patients have not shown an increased risk (28).

Of the drugs available in the United States, quinacrine (Atabrine) is the most effective, with cure rates of 90 to 95%. However, its increased effectiveness in comparison to metronidazole must be weighed against the increased risk of troublesome side effects, tempering enthusiasm for its use as the treatment of choice. The dosages are 100 mg three times a day for 7 days for adults and 2 mg/kg three times a day for children. Compliance is poorer in young children, but the drug may made be more palatable if the appropriate dose is

placed in a gelatin capsule. Common side effects in adults include intestinal upset, headache, and yellow urine. Nausea, vomiting, diarrhea, abdominal cramps, fever, and skin rash are less common side effects that may necessitate discontinuing the drug. Toxic psychosis with either depression or excitation occurs in about 1.5% of adults taking quinacrine (82). Yellowing of the skin and sclerae may rarely occur.

Furazolidone (Furoxone) is the only drug available in liquid form, which makes it useful for infants and young children (51). Cure rates are somewhat less than with metronidazole and quinacrine, being in the 75 to 90% range. Adverse reactions to this drug include gastrointestinal symptoms, fever, rash, and occasionally urticaria, and the urine may become brown. Patients with glucose-6-phosphate dehydrogenase deficiency may develop hemolysis, and an Antabuse-like reaction can occur with alcohol ingestion. Furazolidone has caused mammary tumors in rats and its safety has been questioned; however, it remains an approved drug for giardiasis. The adult dosage is 100 mg four times a day for 7 days, and that for children is 1.25 mg/kg four times a day for 7 days.

In comparative studies outside the United States, tinidazole (Fasigyn) given in a single dose was as effective as drugs available in the United States and was generally better tolerated (35). It is given to adults as a single 2-g dose and as a 30- to 35-mg/kg single dose to children. When available, it is the drug of choice for giardiasis. About 10% of patients experience mild gastrointestinal side effects; headache and vertigo are rarely reported (35, 82).

Asymptomatic cyst passers, particularly young children and food handlers, are potential sources of infection to others and may themselves develop symptoms spontaneously. Although the need to treat asymptomatic carriers is controversial, many physicians prefer to treat all infected individuals living in nonendemic areas.

None of the drugs described here can be used with completely assured safety to the fetus. However, instances may arise in which treatment during pregnancy is necessary, in which case quinacrine is preferred because of its high cure rate. Reports describing treatment of giardiasis with the poorly absorbed antibiotic paromomycin (Humatin) have been mixed, but in one study the drug was shown to be useful when administered to a few pregnant women with the infection (45).

As a check for cure, a series of three stool specimens collected on alternate days should be examined approximately 4 weeks after completion of treatment. With treatment failures, retreatment with a different drug should be attempted.

PREVENTION

Conventional water treatment plants that use coagulation-sedimentation-filtration methods are needed to prevent waterborne giardiasis outbreaks. According to a Centers for Disease Control surveillance report on waterborne disease in the United States between 1986 and 1988, *Giardia* spp. were identified as the causative agent in 9 of 50 outbreaks, the largest of which affected more than 500 people. Eight outbreaks were associated with deficiencies in community water systems, and six were associated with unfiltered surface water systems in which chlorination was the only treatment (46). While chlorination alone is often effective in killing most enteric organisms, *Giardia* cysts may require higher concentrations of chlorine and longer contact times to be inactivated, particularly in cold water (34). For individual protection, bringing water to a rolling boil for 1 min destroys *Giardia* cysts. If boiling is not possible, 2 to 4 drops of household bleach or 0.5 ml of 2% tincture of iodine can be added to each liter of water and the water can be held for 60 min before drinking. A longer treatment time (overnight) is recommended if the water is cold (34). Eating hot, cooked foods helps to prevent ingestion of viable cysts from foods contaminated by infected water or fingers.

Presently, no drugs are available to use for *Giardia* prophylaxis. Considering the many sources from which giardiasis may be acquired, prophylactic therapy may not be of much value except for travel in highly endemic areas.

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